Drug-drug similarity networks for anti-cancer drug discovery – Case studies on Breast Cancer, Colorectal Cancer and Leukemia

Selom Kugbe[1], Zachary Grinslade[1], Salamatu Momoh[1] and **Sara Ibrahim[1]**
Department of Bioinformatics, Indiana University School of Informatics, Indianapolis, IN 46202

Over the decades, the medical industry has been challenged with the issue of producing drugs that would avoid sidetracking to other targets (off-targets) and keep away from harmful side effects (drug adverse reactions). Many researches have shown that complex diseases, such as various cancers, make the "one disease - one target - one drug" strategy unsuccessful due to the intrinsic complexity of gene-gene interactions and gene-environment interactions. In order to discover efficient treatments for these diseases, we assume that optimal drugs should be capable of down-regulating the effects of over-expressed genes while activating the under-expressed genes, when necessary, to restore the patient's status to a healthy one. In this MURI project, we constructed drug-drug similarity network models, as two drugs having similar side effects, targets or chemical structures may have compatible therapeutic effects on the diseases. First, we retrieved a list of top-ranking drugs for specific disease (using Breast Cancer, Colorectal Cancer and Leukemia as case studies) from different data sources of connection maps, including the CMaps webserver. Second, we identified the protein targets for each drugs using databases such as PubChem, MataDor, MetaDrug, the European Bioinformaics Institute, and DrugBank. Third, we calculated similarities between two drugs by using different types of definitions based on their characteristics, such as shared targets, chemical structures, ontology and side effects. Finally, a comprehensive drug-drug similarity network with multiple similarity definitions was created for each disease, through a molecular network visualization platform - Cytoscape. These drug-drug similarity networks for specific cancer phenotypes can be applied to the validation of therapeutic effect assessment for specific anti-cancer drugs based on drug-protein networks. Our research highlights the importance of drug similarity analysis, and will eventually help anti-cancer drug discovery in silico.

Mentors: Jake Chen, Department of Bioinformatics, IU School of Informatics, IUPUI; Xiaogong Wu, Department of Bioinformatics, IU School of Informatics, IUPUI